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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/566,829	01/31/2006	Chikara Jin	TOYA145.001APC	7514

20995 7590 05/29/2009
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EXAMINER

RICCI, CRAIG D

ART UNIT	PAPER NUMBER
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1614

NOTIFICATION DATE	DELIVERY MODE
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05/29/2009

ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No. 10/566,829	Applicant(s) JIN ET AL.	
	Examiner CRAIG RICCI	Art Unit 1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 08 April 2009.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1, 2 and 9 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1, 2 and 9 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Status of the Claims

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 04/08/2009 has been entered.

Response to Arguments



2. Applicants' arguments, filed 04/08/2009, have been fully considered. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. Specifically, the rejections of claims under **(1)** 35 U.S.C. 112, second paragraph, **(2)** 35 U.S.C. 103(a) over *Johnson* in view of *Ninomiya et al*; and **(3)** 35 U.S.C. 103(a) over *Johnson* in view of *Ninomiya et al* in further view of *Hai* are all withdrawn in view of Applicant's amendments to the claims. Since the previous rejections have all been withdrawn, Applicant's arguments as to those rejections are rendered moot. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

4. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

5. **Claims 1 and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over *Ninomiya et al* (cited in a previous Action) in view of *Friedman et al* (Oncologist 5:136-143, 2000), *Nguyen et al* (Annals of Oncology 15:383-388, 2004), *David et al* (Glycerol: A Jack Of All Trades), *Bowen et al* (US 2004/0057908), and *Quercia et al* (cited in a previous Action).**

6. Instant claim 1 has been amended to recite a medicine for oral administration comprising a jellied pharmaceutical composition for oral administration wherein the composition comprises granisetron hydrochloride, a carrageenan (specifically kappa (κ)-carrageenan and/or iota (ι)-carrageenan), locust bean gum, sodium polyacrylate, D-sorbitol, glycerin, and water, wherein the composition has a pH of 7 or less.

7. *Ninomiya et al* teach medicines for oral administration comprising a jellied pharmaceutical composition (Abstract) and which "easily taken by patients of advanced age or patients with dysphagia" (Column 1, Lines 3-4). More specifically, *Ninomiya et al* disclose seven embodiments wherein the composition comprises κ -carrageenan, locust bean gum, sodium polyacrylate, D-sorbitol and water (Columns 10-12, Examples 1-7, Tables 1-5). However,

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Ninomiya et al do not teach compositions comprising (1) granisetron HCl, (2) glycerin and (3) wherein the pH of the composition is 7 or less.

8. **As to (1):** it would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to include granisetron HCl in the jellied pharmaceutical composition taught by *Ninomiya et al*. Although *Ninomiya et al* specifically disclose compositions wherein the medically active ingredient is domperidone (Column 10, Examples 1-2, Table 1), acyclovir (Columns 10-11, Examples 3-4, Table 2), sodium loxoprofen (Column 11, Example 4, Table 3), famatodine (Columns 11-12, Example 6, Table 4) or terfenadin (Column 12, Example 7, Table 5), they also specifically teach that “**any** medically effective components can be used, without particularly being limited” (Column 5, Lines 16-17, emphasis added). Accordingly, the skilled artisan would not have considered the teaching of *Ninomiya et al* to be limited to jellied pharmaceutical compositions comprising only domperidone, sodium loxoprofen, famatodine, or terfenadin, and would have found it *prima facie* obvious to substitute (in place of domperidone, sodium loxoprofen, famatodine, and terfenadin) **any** medically effective ingredient. Moreover, the person of ordinary skill in the art would have found it *prima facie* obvious to use granisetron HCl, specifically, as the medically effective ingredient in the composition taught by *Ninomiya et al*. As evidenced by *Friedman et al*, “5-HT₃-receptor antagonists have become the standard of care for the prevention of acute nausea and vomiting associated with chemotherapy. Granisetron (KYTRIL®, SmithKline Beecham Pharmaceuticals, Philadelphia PA) is effective in preventing nausea and vomiting induced by emetogenic chemotherapy” (Page 137, Column 1). Significantly, KYTRIL® (as taught by *Friedman et al* for the treatment of emesis during chemotherapy) is the hydrochloride salt of granisetron. And,

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as taught by *Nguyen et al*, “[d]ysphagia is a common, debilitating and potentially life-threatening sequela of concurrent chemoradiation for head and neck malignancy” (Abstract). Accordingly, in view of *Ninomiya et al* which, as discussed above, teach that the jellied pharmaceutical composition is “easily taken by patients of advanced age or patients with dysphagia” (Column 1, Lines 3-4) the skilled artisan would have been motivated to provide granisetron HCl (for the treatment of nausea during chemotherapy) in a form which can be easily taken by patients having dysphagia. Accordingly, it would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to use granisetron HCl in the jellied pharmaceutical composition taught by *Ninomiya et al* with a reasonable expectation of success.

9. **As to (2):** it would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to include glycerin in the jellied pharmaceutical composition taught by *Ninomiya et al*. As evidenced by *David et al* (available online at http://www.chem.yorku.ca/hall_of_fame/essays96/glycerol.htm as of April 20, 2001 based on the attached Internet Archive Report), “[a]s a humectant, glycerol constitutes an important pharmaceutical ingredient to prevent the drying out of preparations, particularly ointments and creams” (Paragraph 4). Indeed, *Bowen et al* teach oral gel compositions which may comprise humectants, including glycerin, “in an amount of about 5 to about 90 weight percent, more typically about 10 to about 60 weight percent” (Paragraph 0033). Accordingly, it would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to include glycerin in the jellied pharmaceutical composition taught by *Ninomiya et al*. The skilled artisan would have been motivated to do so in view of *David et al*, in order to prevent the drying out of the jellied preparation taught by *Ninomiya et al* with a reasonable expectation

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of success. Furthermore, in view of *Bowen et al*, the concentration of glycerin recited by instant claim 9 is also *prima facie* obvious. As stated by MPEP 2144.05, “[i]n the case where the claimed ranges ‘overlap or lie inside ranges disclosed by the prior art’” a *prima facie* case of obviousness exists (quoting *In re Wertheim*, 541 F.2d 257 (CCPA 1976)). Thus, since the claimed ranges recited by instant claim 9 lie inside ranges disclosed by the prior art, they are *prima facie* obvious.

10. **And as to (3):** it would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to maintain the pH of the composition to pH 7 or below. Although *Ninomiya et al* do not specifically teach a composition wherein the pH is 7 or less (instead, teaching only that the compositions “retain preservation stability at the medical level in terms of maintenance of appearance and pH” Column 14, Line 67 to Column 15, Line 1), it is well known in the art that the pH of a pharmaceutical composition can influence drug stability, storage and preservation. In particular, *Quercia et al* teach that granisetron HCl in oral liquid formulation is stable in the pH range from 2.7 to 2.8 (Abstract and Page 1406, Column 1, Results Section). Thus it would have been *prima facie* obvious to a person of ordinary skill in the art to formulate the composition taught by *Ninomiya et al* having a pH of 7 or less. In view of *Quercia et al*, the skilled artisan would have found it *prima facie* obvious to formulate the composition comprising granisetron HCl at a pH of 7 or below in order to provide a compositions which retain stability with a reasonable expectation of success.

11. Accordingly, in view of all of the foregoing reasons, instant claims 1 and 9 are rejected as *prima facie* obvious.

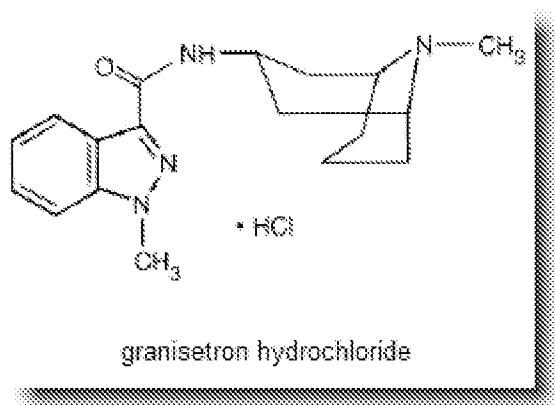
12. Applicant argues that *Ninomiya et al* do not teach compositions containing either granisetron HCl or glycerin and that *Ninomiya et al* do not teach or suggest anything regarding foaming problems (Applicant Argument, Page 5). However, as discussed above, it would have been *prima facie* obvious to include granisetron HCl in the jellied composition to provide formulations for easy administration to patients with dysphagia, and it would have been *prima facie* obvious to include a humectant such as glycerin in the composition to prevent drying of the composition. Thus, the fact that *Ninomiya et al* do not teach foaming problems is not critical since the skilled artisan would have included granisetron and glycerin for the reasons discussed above and which are unrelated to any potential foaming problems. Accordingly, Applicant's argument is not found persuasive.

13. **Claim 2 is rejected under 35 U.S.C. 103(a) as being unpatentable over *Ninomiya et al* (cited in a previous Action) in view of *Friedman et al* (Oncologist 5:136-143, 2000), *Nguyen et al* (Annals of Oncology 15:383-388, 2004), *David et al* (Glycerol: A Jack Of All Trades), *Bowen et al* (US 2004/0057908), and *Quercia et al* (cited in a previous Action) as applied to instant claim 1 above, in further view of *Hai* (cited in a previous Action) and *Shushin et al* (Russian Chem Bull 43:1646-1650, 1994).**

14. Additionally, the composition of *Ninomiya et al* does not teach the inclusion of a reductant as recited by instant claim 2. As discussed in a previous Action, *Hai* teaches that "[t]he desirability of providing pharmaceutical formulations in which an oxidation-susceptible active drug ingredient or ingredients are protected against oxidative degradation inherent to prolonged storage is a concept well known to, and appreciated by, one of ordinary skill in the art. Anti-oxidants commonly employed in various pharmaceutical formulations may include, inter

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alia, vitamin E, ascorbic acid, BHT (butylated hydroxytoluene), BHA (butylated hydroxyanisole), and the like.” In the instant case, granisetron HCl is oxidation-susceptible. Specifically, granisetron HCl, which is represented as having the following structure



encompasses an amide which one of ordinary skill in the art would recognize as susceptible to oxidation in view of *Shushin et al*, which specifically discuss oxidation of amide compounds. Since developing pharmaceutical compositions capable of prolonged storage is desirable, it would have been *prima facie* obvious to a person of ordinary skill in the art to combine a reductant, as taught by *Hai*, with the composition taught by *Ninomiya et al*. As such, instant claim 2 is rejected as *prima facie* obvious.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to CRAIG RICCI whose telephone number is (571) 270-5864. The examiner can normally be reached on Monday through Thursday, and every other Friday, 7:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on (571) 272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/CRAIG RICCI/
Examiner, Art Unit 1614

/Ardin Marschel/
Supervisory Patent Examiner, Art Unit 1614